

Appl. No. : 08/765,837  
Filed : September 7, 1999

### REMARKS

Applicants have amended claims 31-16 and support for the amendment to the claims is found in the specification as filed. Specific support for the term 'human' in the amendments to claims 31, 32 and 35 is found in the specification as filed, see page 10, lines 18-21 and page 11, lines 21-23. Support for the amendment to claim 34 is found on page 18, lines 19-23 and support for the amendment to claim 36 is found on page 18 at lines 31-36.

The following remarks address the substance of the Office Action:

#### I. Matters of definiteness

The Examiner has rejected claims 31, 33, 35, 36 and 39 under 35 U.S.C. § 112, second paragraph on the assertion that the claims are vague and indefinite in their recitation of exact amino acid residues of a genus protein and that the claims as presently recited are not limited to the well known human Factor VIII sequence.

Applicants have amended claims 31 and 35 to recite the phrase "human Factor VIII fragment," thereby addressing the Examiner's concerns by specifying which species the Factor VIII fragments are derived from.

In light of the above remarks, Applicants respectfully request withdrawal of the rejection to claims 31, 33, 35, 36 and 39 under 35 U.S.C. § 112, second paragraph.

#### II. The claimed invention is novel

The Examiner has maintained the rejection of claims 31-36 and 39 under 35 U.S.C. § 102(b) over Capon et al. (USP 4,965,199) on the assertion that the claims read on the full length Factor VIII protein. The foregoing amendments limit the claims to antigenic fragments or epitopes of the human Factor VIII protein. Applicants maintain that the cited reference contains no recitation of antigenic epitopes within the human Factor VIII protein nor does it disclose antigenic fragments of the human Factor VIII protein.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection to claims 31-36 and 39 under 35 U.S.C. § 102(b).

#### III. Conclusion

Applicants have amended claims 31-36 and these changes made to the claims by the current amendment, including insertions and **[deletions]**, are shown on an attached sheet

Appl. No. : 08/765,837  
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entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this amendment. No new matter has been added herewith.

If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: \_\_\_\_\_

12/26/02

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Appl. No. : 08/765,837  
Filed : September 7, 1999

31. **(Twice Amended)** An antigenic **[polypeptide comprising]** fragment of the human Factor VIII polypeptide, said fragment comprising at least 7 amino acids of a human Factor VIII fragment selected from the group consisting of a human Factor VIII fragment contained between arginine 1652 and arginine 1696 inclusive, a human Factor VIII fragment contained between threonine 1739 and aspartic acid 1831 inclusive, and a human Factor VIII fragment contained between glutamic acid 1885 and arginine 1917 inclusive.

32. **(Twice Amended)** **[An]**The antigenic polypeptide according to Claim 31, wherein said human Factor VIII fragment comprises an epitope selected from the group consisting of:

a human Factor VIII fragment contained between arginine 1652 and tyrosine 1664 (SEQ ID No:1), [a Factor VIII fragment contained between aspartic acid 1681 and arginine 1696 (SEQ ID No:2), ]a human Factor VIII fragment contained between threonine 1739 and tyrosine 1748 (SEQ ID No:3), a human Factor VIII fragment contained between asparagine 1777 and phenylalanine 1785 (SEQ ID No:4), a human Factor VIII fragment contained between glutamic acid 1794 and tyrosine 1815 (SEQ ID No:5), a human Factor VIII fragment contained between methionine 1823 and aspartic acid 1831 (SEQ ID No:6), a human Factor VIII fragment contained between glutamic acid 1885 and phenylalanine 1891 (SEQ ID No:7), a human Factor VIII fragment contained between glutamic acid 1893 and alanine 1901 (SEQ ID No:8), and a human Factor VIII fragment contained between aspartic acid 1909 and arginine 1917 (SEQ ID No:9).

33. **(Twice Amended)** **[An]**The antigenic polypeptide according to Claim 31, wherein said antigenic polypeptide comprises tyrosine or histidine.

34. **(Twice Amended)** A conformational epitope containing at least two different human Factor VIII fragments[epitopes of the antigenic polypeptide] of Claim 32, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

Appl. No. : 08/765,837  
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35. **(Twice Amended)** A conformational epitope containing at least two different epitopes from a human Factor VIII fragment selected from the group consisting of a human Factor VIII fragment contained between arginine 1652 and arginine 1696 inclusive, a human Factor VIII fragment contained between threonine 1739 and aspartic acid 1831, inclusive, and a human Factor VIII fragment contained between glutamic acid 1885 and arginine 1917 inclusive.

36. **(Twice Amended)** A complex comprising a carrier protein or a carrier peptide linked to the antigenic polypeptide of Claim 31 or the conformational epitope of Claim 35, whereby said complex increases immunogenicity.